

# **Influenza A (H3N2) Variant Virus (also known as “H3N2v”) - Key Points**

August 3, 2012

## **In this document:**

- [Influenza A\(H3N2\) Variant Virus \(also known as “H3N2v”\)](#)
  - [Summary of Epidemiology of H3N2v Cases to Date](#)
  - [What Could Happen \(More Cases May Occur, Some Severe\)](#)
- [CDC Information/Recommendations, Including Treatment](#)
  - [CDC Recommendations for the Public](#)
  - [Information for People Attending Fairs](#)
  - [Signage for Posting at Fairs and Other Places Animals are Exhibited](#)
  - [CDC Guidance Documents](#)
- [CDC Preparedness Activities](#)
  - [H3N2v Vaccine Virus Candidate](#)
  - [Diagnostic Tests for Detecting H3N2v Viruses](#)
  - [Antiviral Susceptibility](#)
  - [Genetic Characterization](#)
  - [Transmissibility and Virulence](#)
  - [Population Immunity](#)
  - [Surveillance for Cases](#)
  - [Communication and Partner Outreach](#)
- [Influenza in Swine: Background](#)
- [Reporting of Human Infections with Novel Influenza A Viruses](#)

## **Influenza A(H3N2) Variant Virus (also known as “H3N2v”)**

- Influenza A (H3N2) viruses with genes from avian, swine and human viruses that normally circulate in swine can sometimes infect humans.
- When human infections with these viruses occur, these viruses are called “variant” viruses (which can also be denoted with the letter “v”).
- When these viruses are found in swine, they are called swine influenza A (H3N2) viruses.
- In 2011, a new influenza A (H3N2v) virus was detected that had acquired the M gene from the influenza A(H1N1)pdm09 (2009 H1N1) virus.
- Sporadic human infections with this H3N2v virus have been detected (see Summary of Epidemiology).
- Most human infections have occurred following swine contact. While limited human-to-human transmission of H3N2v virus is thought to have occurred on three occasions in the fall and winter of 2011, sustained and efficient community transmission of H3N2v virus has not been detected to date.

## **Influenza A (H3N2) Variant Virus (also known as “H3N2v”) - Key Points**

**August 3, 2012**

- According to USDA swine influenza surveillance, this swine H3N2 virus with the pandemic M gene has been detected in swine in a number of U.S. states. This virus may be circulating widely in U.S. swine at this time.
- It is possible that acquisition of the 2009 H1N1 virus M gene may make H3N2 viruses in swine more transmissible to humans and possibly among humans.

### **Summary of Epidemiology of H3N2v Cases to Date**

- On August 3, CDC’s FluView U.S. Weekly Influenza Surveillance Report announced 12 new cases of H3N2v virus infection from three states: Hawaii (1), Indiana (1) and Ohio (10).
- From July 12 through August 1, 2012, 16 confirmed cases of H3N2v virus were reported to CDC. (These 16 cases include four cases from Indiana reported previously in the July 27<sup>th</sup> FluView and MMWR). Of these 16 cases:
  - All 16 cases reported contact with swine prior to illness onset;
  - 15 reported contact while attending or exhibiting swine at an agricultural fair.
- To date since July 2011,
  - 29 cases of human infection with H3N2v virus (containing the 2009 H1N1 virus M gene) have been detected from eight states: Hawaii (1), Indiana (7), Iowa (3), Maine (2), Ohio (10), Pennsylvania (3), Utah (1), and West Virginia (2);
  - 3 patients were hospitalized as a result of their illness in 2011, and all have recovered;
  - 23 of these cases reported swine contact prior to onset of their illness;
  - Of these 23 cases, 19 were associated with fairs where swine were present;
  - In 6 cases (all reported in 2011), there was no reported swine contact.
- All of the persons hospitalized as a result of their H3N2v illness in 2011 had underlying health conditions that would predispose them to more serious influenza-related illness. (The full list of people at greater risk of serious influenza-related complications is available at [http://www.cdc.gov/flu/about/disease/high\\_risk.htm](http://www.cdc.gov/flu/about/disease/high_risk.htm).)
- Most cases of H3N2v virus infection have occurred in children. A few adult cases have been reported.
- Cases have been identified following:

## **Influenza A (H3N2) Variant Virus (also known as “H3N2v”) - Key Points**

**August 3, 2012**

- Exposure to swine, (swine-to-human transmission; e.g., direct contact, close contact – such as walking in a barn with sick pigs)
- Exposure to people with swine exposure, (limited human-to-human transmission).
- Exposure to people with influenza-like-illness (ILI) in child care settings with no clear linkage to swine, (limited human-to-human transmission).
- No sustained (ongoing) community transmission of H3N2v virus has been observed at this time.
- While still rare, H3N2v virus infections have been identified with greater frequency than previous human infections with variant influenza viruses.
- CDC is monitoring the situation closely.
- An H3N2v vaccine candidate was prepared and two trial lots of vaccine have been produced. Clinical trials are planned later in 2012.

### **What Could Happen? (More Cases May Occur, Some Severe)**

- More cases of human infection with H3N2v virus are anticipated, occurring either from exposure to infected swine or through subsequent, limited human-to-human transmission.
- Limited serologic studies conducted to date indicate that children would have little to no pre-existing immunity to this new virus (whereas, adults may have some pre-existing immunity). Therefore, cases are more likely to occur in children.
- Also, as with seasonal influenza, certain people are likely at greater risk of serious influenza-related complications.
- As a result, cases of severe illness and death resulting from infection with this virus could occur among children and other people, especially those with high risk conditions like asthma, diabetes, heart disease or women who are pregnant.
- It also is possible that this H3N2v virus could gain increased capacity for efficient and sustained human-to-human transmission because influenza viruses are constantly evolving.

### **CDC Information/Recommendations, Including Treatment**

## Influenza A (H3N2) Variant Virus (also known as “H3N2v”) - Key Points

August 3, 2012

- In response to recent human cases of H3N2v virus infection, CDC would like to convey the following information:
  - (1) CDC recommends annual seasonal influenza vaccination for all persons aged 6 months and older to protect against seasonal influenza viruses; however, seasonal influenza vaccine is unlikely to protect against variant influenza viruses, including H3N2v viruses.
  - (2) Studies conducted by CDC have indicated that children younger than 10 years old would have little to no immunity against H3N2v virus, whereas adults may have some cross-protective immunity. Most cases of H3N2v have occurred in children at this time.
  - (3) There are two FDA-approved prescription antiviral drugs that are expected to be effective in treating illness associated with H3N2v. The antiviral drugs oseltamivir (Tamiflu) and zanamivir (Relenza) – which are used to treat infection with seasonal influenza viruses – are also expected to be effective in treating H3N2v virus infection. Early initiation of antiviral treatment is most effective. (For more information about influenza antiviral medications, please see [www.cdc.gov/flu/antivirals/whatyoushould.htm](http://www.cdc.gov/flu/antivirals/whatyoushould.htm).)
  - (4) Influenza variant viruses have not been shown to be transmissible to people through eating or proper handling of pork (pig meat) or other products derived from pigs. For more information about the proper handling and preparation of pork, visit the USDA website fact sheet “[Fresh Pork from Farm to Table](#).”

### CDC Recommendations for the Public

- At this time, CDC recommends the following:
- If you go to a doctor for flu symptoms (see below) following direct or close contact with swine, tell your doctor about this exposure.
- If you have flu symptoms, follow **CDC’s regular recommendations for seeking treatment for influenza**.
  - a. If you have symptoms of flu and are very sick or worried about your illness contact your health care provider.
  - b. Certain people are at greater risk of serious flu-related complications (including young children, elderly persons, pregnant women and people with certain long-term medical conditions) and this is true both for seasonal flu and novel flu virus infections. (For a full list of people

## **Influenza A (H3N2) Variant Virus (also known as “H3N2v”) - Key Points**

**August 3, 2012**

at higher risk of flu related complications, see  
[www.cdc.gov/flu/about/disease/high\\_risk.htm](http://www.cdc.gov/flu/about/disease/high_risk.htm).)

- If these people develop ILI, it's best for them to contact their doctor as soon as possible. (The majority of recent H3N2v cases have been in children.)
- c. Your doctor may prescribe antiviral drugs that can treat the flu, including H3N2v. These drugs work better for treatment the sooner they are started. If you are prescribed antiviral drugs by your doctor, you should finish all of the medication, according to your doctor's instructions.
- Also, whenever you have flu symptoms and are seeing a health care provider, always remember to tell them if you have asthma, diabetes, heart disease, neurological and neurodevelopmental conditions, are pregnant, or are older than 65 or younger than 5 years. These conditions and age factors put you at high risk of serious complications if you have the flu.
- Flu signs and symptoms usually include fever and respiratory symptoms, such as cough and runny nose, and possibly other symptoms, such as body aches, nausea, vomiting, or diarrhea.
- Health care providers will determine whether influenza testing and possible treatment are needed.
- There are antiviral drugs that can be used to treat H3N2v as well as seasonal influenza. More information about influenza antiviral drugs is available at [Treatment \(Antiviral Drugs\)](#).

### **Information for People Attending Fairs**

- Thousands of fairs take place across the United States each year. Swine exhibits are common at these fairs.
- Of the H3N2v cases reported since July 2012 to date, 15 of 16 have been associated with attendance at fairs where swine were present. In some cases, patients reported direct contact with swine, in other cases they did not.
- CDC would like to let people know about some preventative actions they can take to make their fair experience a safe and healthy one.
- The National Association of State Public Health Veterinarians has developed the [“Compendium of Measures to Prevent Disease Associated with Animals in Public Settings, 2011](#), available online at <http://nasphv.org/documentsCompendiumAnimals.html>, to provide some

## Influenza A (H3N2) Variant Virus (also known as “H3N2v”) - Key Points

August 3, 2012

preventive actions that are applicable to people raising animals, showing animals at fairs, or attending fairs including swine.

- **Take Action to Prevent the Spread of Flu Viruses Between People and Pigs**
  - Wash your hands frequently with soap and running water before and after exposure to animals.
  - Never eat, drink or put things in your mouth while in animal areas and don't take food or drink into animal areas.
  - Children younger than 5 years, people 65 years and older, pregnant women, and people with certain chronic medical conditions (like asthma, diabetes, heart disease, weakened immune systems, and neurological or neurodevelopmental conditions) are at high risk from serious complications if they get influenza. **These people should consider avoiding exposure to pigs and swine barns this summer, especially if sick pigs have been identified.**
  - If you have animals – including swine – watch them for signs of illness and call a veterinarian if you suspect they might be sick.
  - Avoid close contact with animals that look or act ill, when possible.
  - Avoid contact with pigs if you are experiencing flu-like symptoms.
  - If you must come in contact with pigs while you are sick, or if you must come in contact with pigs known or suspected to be infected, or their environment, you should use appropriate protective measures (for example, wear protective clothing, gloves, masks that cover your mouth and nose, and other personal protective equipment) and practice good respiratory and hand hygiene.

### Signage for Posting at Fairs and Other Places Animals are Exhibited

- The “Compendium of Measures to Prevent Disease Associated with Animals in Public Settings, 2011” states that education is essential to reduce risks associated with animal contact in public settings and claims that experience from outbreaks suggests that visitors knowledgeable about potential risks are less likely to become ill. The compendium offers the following recommendations to venue operators regarding signage and hand washing recommendations:
- Venue operators should:
  - Maintain hand-washing stations that are accessible to children, and direct visitors to wash their hands when exiting animal areas.

## Influenza A (H3N2) Variant Virus (also known as “H3N2v”) - Key Points

August 3, 2012

- Position hand-washing stations in places that encourage hand washing when exiting animal areas.
  - Provide visitors with educational messages before they enter the exhibition areas, including information that animals can cause injuries or carry organisms that can cause serious illness.
  - Provide information in a simple and easy-to-understand format that is age- and language-appropriate.
  - Provide information in multiple formats (e.g., signs, stickers, handouts,).
- The Compendium provides posters for use around animal exhibits that describe actions people can take to minimize disease and injury risks. These materials include:
  - Safety at Animal Exhibits Poster (<http://nasphv.org/Documents/AnimalExhibitsSafety.pdf>)
  - Animal Exhibits Handwashing Poster (<http://nasphv.org/documentsCompendiumAnimals.html>)
  - Animal Exhibits Handwashing Poster (Spanish) (<http://nasphv.org/Documents/HandwashingPosterSpanish.pdf>)
- Several state agencies have made additional signage publicly available:
  - The North Carolina Department of Agriculture & Consumer Services has animal exhibit signage publicly available on its website at <http://www.ncagr.gov/markets/fairs/fairmanagerinfo.htm#resources>.
  - The Colorado Department of Public Health and Environment has animal exhibit signage publicly available on its website at ([http://www.cdphe.state.co.us/dc/Epidemiology/dc\\_group.html](http://www.cdphe.state.co.us/dc/Epidemiology/dc_group.html)) under the “Animals in Public Settings” heading.

### CDC Guidance Documents

- Guidance documents related to variant influenza viruses, such as H3N2v are posted at <http://www.cdc.gov/flu/swineflu/influenza-variant-viruses.htm>.
- These guidance documents are:
  - “Interim Guidance on Case Definitions to be Used for Investigations of Influenza A (H3N2) Variant Virus Cases” for state and local health departments is available at <http://www.cdc.gov/flu/swineflu/case-definitions.htm>.
  - “Prevention Strategies for Seasonal and Influenza A(H3N2)v in Health Care Settings” is available at <http://www.cdc.gov/flu/swineflu/prevention-strategies.htm>.

## Influenza A (H3N2) Variant Virus (also known as “H3N2v”) - Key Points

August 3, 2012

- “Interim Guidance on Specimen Collection, Processing and Testing for Patients with Suspected Influenza A (H3N2) Variant Virus Infection” for public health professionals is available at <http://www.cdc.gov/flu/swineflu/h3n2v-testing.htm>, and
- “Interim Guidance for Influenza Surveillance: Additional Specimen Collection for Detection of Influenza A (H3N2) Variant Virus Infections” for state and local health departments is available at <http://www.cdc.gov/flu/swineflu/h3n2v-surveillance.htm>.

### CDC Preparedness Activities

#### *H3N2v Virus Vaccine Candidate:*

- One routine pandemic preparedness measure is development of a candidate vaccine virus that could be used to produce a vaccine.
- There are many steps involved with producing an influenza vaccine, the first being development of a vaccine candidate virus.
- CDC identified an egg-grown wild-type H3N2v virus isolated from a human case in 2010 and sent this virus to New York Medical College where a high-growth candidate vaccine was made.
- This virus did not possess the matrix M gene from the 2009 H1N1 virus, however, laboratory data show that a vaccine made from this virus would protect against H3N2v viruses, including those with the M gene from the 2009 H1N1 virus.
- The scientific nomenclature for this vaccine virus is “A/Minnesota/11/2010.”
- A high-growth or high-yield virus is a reassortant virus that is used to grow the virus in mass quantities for vaccine production.
- CDC has provided the candidate vaccine virus to World Health Organization (WHO) Collaborating Centers, the essential regulatory laboratories (including FDA), and to vaccine manufacturers. Distribution of the vaccine virus began on September 14, 2011 (to FDA). By October 31, 2011 all the WHO Collaborating Centres and four vaccine manufacturers had received the vaccine virus.
- CDC also entered shipments of these viruses into the WHO [Influenza Virus Tracking Mechanism](https://extranet.who.int/ivtm/Default.aspx) (IVTM). More information is available at <https://extranet.who.int/ivtm/Default.aspx>.
- According to HHS, clinical investigational lots of two inactivated subunit H3N2v vaccines have been made by manufacturers using different technologies (egg- and cell-based).
- Formulation and fill finish manufacturing of the vaccines will be completed, and clinical trials using the NIH’s Vaccine and Therapeutics Evaluation Unit (VTEU) will follow in 2012.



## Influenza A (H3N2) Variant Virus (also known as “H3N2v”) - Key Points

August 3, 2012

- Candidate vaccine viruses have been developed in the past when human infections with other novel influenza A virus infections have occurred. For example, candidate vaccines have been prepared against H9N2, H7N7 and several different H5N1 viruses for pandemic preparedness.

### *Diagnostic Tests for Detecting H3N2v Viruses*

- The CDC real time reverse transcription polymerase chain reaction (rRT-PCR) assay that was approved by FDA in September 2011 is able to accurately identify cases as presumptive H3N2v cases. The assay can detect the gene for the H3 hemagglutinin which has a human (or swine) origin as well as the NP nucleoprotein gene which has a swine origin.
- CDC rRT-PCR kits have been distributed to U.S. public health laboratories and National Influenza Centers in other countries. Increased production of these kits is available for surge response if needed.
- Additional polymerase chain reaction (PCR) test enhancements to optimize detection of H3N2v virus are under development.
- Commercially available rapid influenza diagnostic tests (RIDTs) **may not** detect H3N2v virus in respiratory specimens. In addition, a positive test result for influenza A cannot confirm H3N2v virus infection because these tests cannot distinguish between influenza A virus subtypes (does not differentiate between human influenza A viruses and H3N2v virus).

### *Antiviral Susceptibility*

- There are two FDA-approved drugs that are expected to be effective in treating illness associated with H3N2v. The antiviral drugs oseltamivir (Tamiflu) and zanamivir (Relenza) – which are used to treat infection with human seasonal influenza viruses –are also expected to be effective in treating H3N2v virus infection. Early initiation of antiviral treatment is most effective. (For more information about influenza antiviral medications, please see [www.cdc.gov/flu/antivirals/whatyoushould.htm](http://www.cdc.gov/flu/antivirals/whatyoushould.htm).)
- All variant influenza viruses are evaluated for antiviral susceptibility. All H3N2v viruses identified in human cases evaluated to date are susceptible to the commercially available neuraminidase inhibitors oseltamivir (Tamiflu®) and zanamivir (Relenza®). So far all the H3N2v viruses are resistant to the adamantane class of drugs (amantadine, rimantadine).
- CDC has deployed antiviral susceptibility testing at several public health departments and at CDC labs. The pyrosequencing test used for human influenza A (H3N2) viruses is suitable for testing the H3N2v virus as well.

### *Genetic Characterization*

- All 29 human cases of H3N2v virus infection since 2011 have had full or partial gene sequencing performed.

## **Influenza A (H3N2) Variant Virus (also known as “H3N2v”) - Key Points**

August 3, 2012

- Available sequences are posted on publicly available gene databases (including [GISAID](#)) in coordination with the FluView publication for researchers and others to use.

### ***Transmissibility and Virulence***

- Ferrets infected with H3N2v viruses before they acquired the M gene demonstrated that the virus grew efficiently in the ferret’s upper respiratory tract, caused disease in the ferrets, and was efficiently transmitted from one ferret to another by both direct contact and respiratory droplet transmission.
- Glycan array binding studies demonstrated that these viruses possessed human-like ( $\alpha$ 2-6 linked) receptor-binding properties.

### ***Population Immunity***

- A CDC serology study published in an April 2012 Morbidity and Mortality Weekly Report (MMWR) investigated whether human populations had existing antibodies that could “recognize” and target H3N2v viruses.
- The study also examined whether seasonal influenza vaccination (with vaccine formulated to protect against seasonal influenza viruses in humans, not H3N2v viruses) can result in development of antibodies capable of recognizing and targeting H3N2v viruses. Such antibodies, which are produced by the immune system to recognize and target one virus, but that also can recognize and target different viruses, are called “cross reactive” antibodies.
- This study showed that seasonal influenza inactivated vaccine (flu shot) is not expected to protect against H3N2v virus in young children, and will only provide limited protection against H3N2v virus in adults.
- If the H3N2v virus acquired the ability to spread easily among humans, children younger than 10 years of age are likely to be the most susceptible to infection with H3N2v viruses.
- In this small study, cross reactive antibodies to H3N2v virus were detected in less than half of people aged 10-49 years. Since this was a limited study, additional investigations of cross-reactive antibodies and susceptibility to H3N2v virus infection are needed, especially in older adults.
- An H3N2v-specific influenza vaccine would provide the best protection against H3N2v viruses.
- This study, entitled: “Antibodies Cross-Reactive to Influenza A (H3N2) Variant Virus and Impact of 2010–11 Seasonal Influenza Vaccine on Cross-Reactive Antibodies — United States,” is available online at <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6114a1.htm>.

### ***Surveillance for Cases***

- CDC is working with the Council of State and Territorial Epidemiologists (CSTE) to support rapid investigations and reporting of potential H3N2v cases.

## **Influenza A (H3N2) Variant Virus (also known as “H3N2v”) - Key Points**

August 3, 2012

- Enhanced surveillance has been established in areas near laboratory-confirmed H3N2v cases.

### ***Communications and Partner Outreach***

- CDC is providing routine and timely communications surrounding H3N2v human cases with the public, partners, state and local health departments and stakeholders, including coordinated publication in FluView, CDC websites, and key points.
- CDC has updated the swine influenza general brochure “What People Who Raise Pigs Need to Know about Influenza” in coordination with USDA and the National Pork Board.
- The National Center for Immunization and Respiratory Diseases (NCIRD) and The National Center for Emerging and Zoonotic Infectious Diseases (NCEZID) at CDC are engaging 4H clubs at the national and state level to develop training materials for enhancing awareness of swine influenza and other zoonotic infections.
- More information about swine influenza and links to all previous reports related cases of H3N2v virus infections are available on the CDC swine influenza website at [www.cdc.gov/flu/swineflu/index.htm](http://www.cdc.gov/flu/swineflu/index.htm).

### **Influenza in Swine: Background**

- Influenza A virus infections are common in pigs, but influenza A viruses that commonly spread in pigs are generally different from the ones that spread in humans.
- Many of the influenza A viruses that normally circulate in pigs can cause infection in people, but this is not common.
- When people are infected with influenza A viruses that are known to be genetically similar to viruses circulating in swine, these viruses are called “variant viruses.” In 2005 and 2006, three cases of infection with influenza viruses that normally circulate in swine (“variant viruses”) were reported in people.
- Beginning in 2007, about three to four of these cases were reported per year. This increased reporting may partially be because human infection with novel (non-human) influenza A viruses became nationally notifiable in 2007 and because improved testing at public health laboratories was initiated. That means that when a human infection due to a non-human influenza A virus is detected in people, it must be reported to federal and the World Health Organization (WHO) authorities.

## **Influenza A (H3N2) Variant Virus (also known as “H3N2v”) - Key Points**

August 3, 2012

- In 2011, 14 cases of variant viruses were reported; 12 of these cases were H3N2 variant viruses. Two of the 12 cases were from Indiana.
- From the cases investigated to date, when people are infected with variant viruses, the signs and symptoms have been basically the same as those caused by illness from human influenza viruses and can include fever, cough, sore throat, body aches, headaches, fatigue and runny or stuffy nose. There may also be vomiting or diarrhea.
- Investigations of human cases of infection with variant viruses are a part of recommended public health practice for this notifiable disease. These investigations are designed to determine if the variant virus in question is spreading from person to person.
- H3N2v viruses have not been shown to be transmissible to people through eating or proper handling of pork (pig meat) or other products derived from pigs. For more information about the proper handling and preparation of pork, visit the USDA website fact sheet [Fresh Pork from Farm to Table](http://www.fsis.usda.gov/factsheets/Pork%20From%20Farm%20to%20Table/index.asp) at <http://www.fsis.usda.gov/factsheets/Pork From Farm to Table/index.asp>.

### **Reporting of Human Infections with Novel Influenza A Viruses**

- In 2007, human infection with a novel influenza A virus became a nationally notifiable condition in the United States.
- In the same year, the International Health Regulations (IHR) were adopted, which requires countries to report certain disease outbreaks and public health events to the World Health Organization (WHO), including any confirmed case of human infection with a novel influenza A virus.
- Novel influenza A virus infections include all human infections with influenza A viruses that are different from currently circulating human influenza H1 and H3 viruses. These viruses include those that are subtyped as non-human in origin and those that are unsubtypable with standard methods and reagents.
- An International Health Regulation (IHR) report is submitted to the World Health Organization when an influenza variant virus case is confirmed.
- Domestically, states report cases of novel influenza A virus infection to the [National Notifiable Disease Surveillance System \(NNDSS\)](#).
- CDC then reports (domestic) cases publicly in [FluView](#).
- Genetic sequence information for these viruses is then posted to GISAID ([www.gisaid.org/](http://www.gisaid.org/)) and GenBank.